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Neonatal References: Epidemiology and Prognosis in a Malian Context

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Abstract

Neonatal mortality remains a public health problem in Mali. The neonatal referral is a systemic factor determining the neonatal prognosis. This work was initiated to determine the frequency of neonatal referrals and to determine their prognosis. **Patients and Methods:** A cross-sectional study was carried out from November 1, 2019 to January 31, 2020 in the neonatology service of the pediatrics department of the Gabriel Toure University Hospital in Bamako. All newborns referred by another health structure in the country were included in this stud. All newborns referred by another health structure in the country were included in this study. To determine the risk factors related to the neonatal referral, we performed univariate and multivariate analyzes to determine the odds ratios and fitted with a significant p probability if p < 0.05 and the 95% confidence interval. **Results:** The frequency of referrals was 54.3%. Newborns came from basic structures in 19.3% of cases, from tertiary structures in 6.7%. The main reason for transfer was prematurity (40.2%) followed by perinatal anoxia (15.3%), malformations (15.3%), respiratory distress (15.2%) and infection neonatal (9.1%). The ambulance was the primary means of transfer in 71.3%. In 80% of cases the transfer had been made within the first 24 hours of life. On admission, a third of the newborns (31.1%) were less than 1500 g, hypothermic in 43.8% and febrile in 15.1%. The evolution was marked by 40.2% of deaths. The analysis of prognostic factors, allowed us to observe that the more the newborn is premature or of low weight the more risk of death was very high with respectively 18.5 times

in the less than 28 weeks of amenorrhea (WA) (ORa = 18.5; CI = 1.9 - 180; p = 0.012) and 6.6 times in those less than 1000g (ORa = 6.6; CI = 1.4 - 29.7; p = 0.015). Likewise, any change in body temperature increased risk of death by 1.9 times compared to normothermia. **Conclusion:** The establishment of a neonatal referral system is necessary to reduce neonatal mortality in our context.

Keywords

Neonatal References, Epidemiology, Prognosis, Malian Context

1. Introduction

Neonatal reference is the transfer of a newborn at a higher level for review and or care. It requires a rigorous organization by a prior call from the reception structure, a means of medical transport and competent medical and paramedical staff to ensure a referral in the best conditions [1] [2] [3]. In France, the organization of perinatal care, on the basis of a regional network, allows *in utero* transfer of the mother-fetus couple at an optimal level to ensure their complete care. This network organization has enabled a very significant reduction in the number of postnatal referrals [4] [5] [6]. In Mali, the reference system/evacuation of obstetric emergencies has been established since 1993 resulting in a positive impact in reducing maternal mortality [7] [8]. However, it was not until 2002 that the newborn was introduced into this system. Despite everything, neonatal mortality still remains high in our country [7] [8]. Because the system has remained in an embryonic state due to the fact that neonatal references are made without any prior organization and the means of transport are inadequate [7] [8] [9]. In setting up the referral/neonatal evacuation system, the optimal level of care expected must be defined by level of the health pyramid. The Gabriel Toure University Hospital Center is located at the top (tertiary level) of the health pyramid of Mali, which houses within it the country's reference neonatal service ensuring the activities of a neonatal service, neonatal intensive care and neonatal resuscitation [10]. Neonatal mortality remains very high from 28.5% to 36.8% [9] [10]. And referrals represent around 60% to 85% of our hospitalizations [9] [10] [11] [12]. We receive newborns from all health structures in Bamako and the different regions of the country. It is evident that improving the conditions of transport and transfer of the vitally distressed newborn is an essential factor in reducing neonatal mortality [13] [14]. Thus the reference constitutes a determining factor of the neonatal prognosis. It is with this vision that this work was initiated in order to determine the frequency of neonatal references and clarify their prognosis.

2. Patients and Methods

This study took place in the referral neonatal service in Mali, which was created

in 1999. Until December 2007, it was a resuscitation service providing care for children in vital distress as well as newborns. With annual number of hospitalizations of 4000 infants, or 43% of hospitalizations of pediatric department and 23% of all Gabriel Toure University Hospital [11]. We carried out a cross-sectional study over a 3-month period from November 1, 2019 to January 31, 2020 in the neonatology service of the pediatrics department of the Gabriel Toure university hospital center. All newborns referred by another health structure in the country were included. We have excluded all referrals or transfers from the maternity the Gabriel Toure University Hospital, all births at home and newborns brought by their parents. We calculated a minimum sample size (*n*) by Schwartz's formula: $n = Z(\alpha)^2 \, pq/i^2$ and we took the prevalence p at 71% from the study carried out in the service in 2010 [9] and we found a minimum number of 360 newborns. The variables studied were: gender, residence, source structure, reference purposes, the means of transport used, the consultation period, gestational age (GA), weight, temperature and become immediate. Data collected retrospectively from newborn medical records and service registers. Analysis was done by Statistical Package for Social Sciences (SPSS) version 22. Descriptive analysis was done to determine the frequency of categorical variables. Univariate analysis and logistic regression were performed to determine the neonatal mortality determinants related to the reference. The binary logistic regression at various levels has been adjusted to identify significant neonatal mortality determinants associated with the reference of the newborn, adjusted odds ratio (OR a) with confidence interval (CI) of 95% and p < 0.05 demonstrated that the determinants were statistically significant.

3. Results

3.1. Patient Characteristics and Sociodemographic Conditions of Transfer

During the study period, referrals represented 54.3% of hospitalized patients, or 450 out of the 828 newborns in hospital. The sex ratio was 1.4 in favor of the male sex. The most represented places of residence were commune I of the district of Bamako (21.7%), commune IV (10%) and the circle of Kalaban Coro (15.1%). Regarding the structures from which our patients came, from Bamako the patients mainly came from secondary health centers: the Reference Health Centers (RHC) of the district in 50.9% of cases (especially the CI RHC: 21.6% and the RHC CV: 9.6%). Basic health centers: private structures (Clinics/Medical Cabinets) in 12.4% and Community Health Centers (CHC) represented 6.9% of referrals. Tertiary structures (hospitals) sent us 6.7% of our patients. The top five referral reasons were prematurity and its complications (40.2%), perinatal anoxia (15.3%), malformations (15.3%), respiratory distress (15.2%) and neonatal infections (9.1%). In addition to these reasons, the lack of space or oxygen constituted 9.6% of reasons for transfer to the RHC level. Malformations made up the bulk of referrals from other health facilities in the country (32%). The means of

transport used were ambulance (71.3%), taxi (26.2%) and personal vehicle (2.5%). The ambulance was the means of transport most used by the secondary health structures of RHC (89%) and tertiary (93%) of the country. The taxi was used by private structures (82%) and CHC (93%) (Figure 1).

3.2. Clinical Characteristics of the Patient

The average transfer time was 18 hours with 80% of referrals made in the first 24 hours, 67.6% of which were before the sixth hour of life. Regarding gestational age (GA) birth, the majority were born prematurely (50.7%) of which 6.4% before the 28th WA. For the admission weight, one third (31.1%) were less than 1500 g with 8.4% less than 1000 g. On arrival, 43.8% of the newborns were hypothermic (<36°C) and 15.1% were febrile. For the prognosis, the immediate course was marked by 40.2% of deaths. Analysis of mortality according to the structure of origin, we found that 46.8% of references from the interior of the country died, followed by private structures (44.6%), RHC of the district (40.2%), CHC (38.7%), Kati structures (33.3%) and hospitals (30%). For referral reasons, nearly half (48.7%) referred for neonatal infection died followed by prematurity (44.2%), respiratory distress (42.6%), malformations (36.2%) and perinatal anoxia (27.5%) (Figure 2).

3.3. Prognostic Factors Influencing Mortality

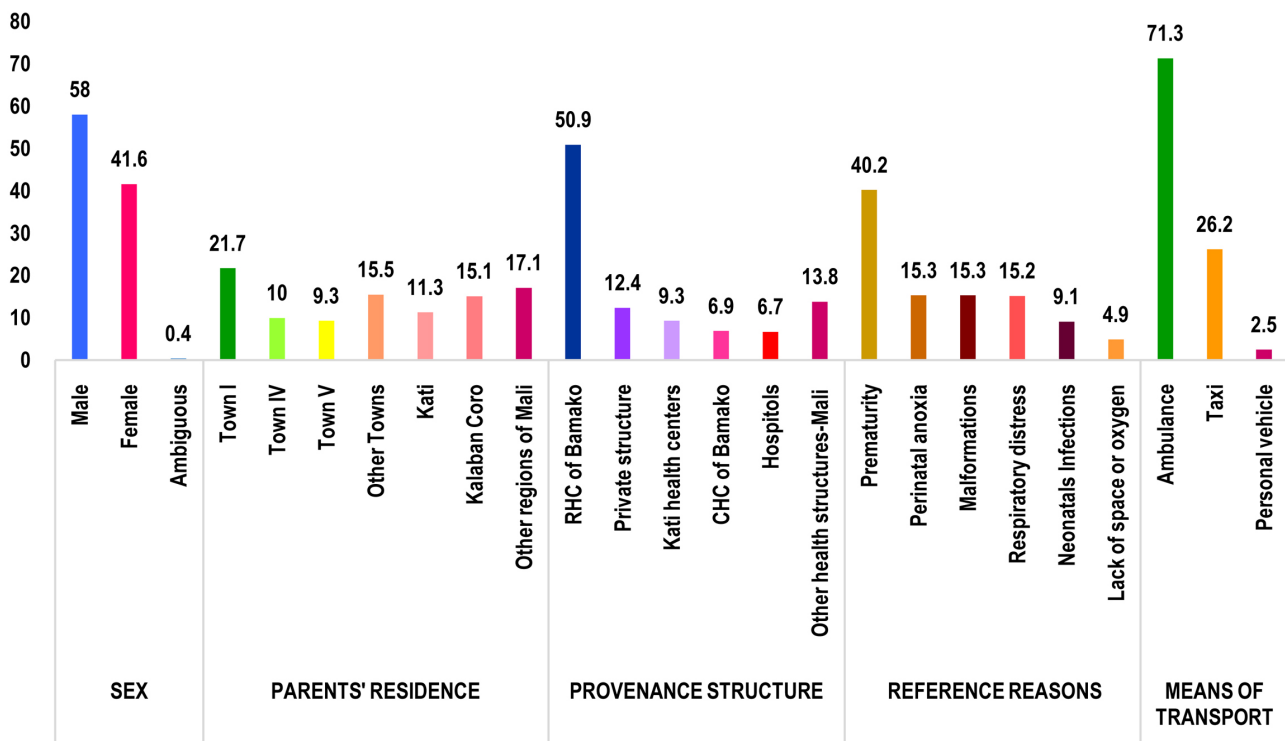By doing univariate analysis and logistic regression of certain prognostic factors,

Figure 1. Distribution of patients according to: gender, residence, structure of origin, reason for referral and means of transport used.
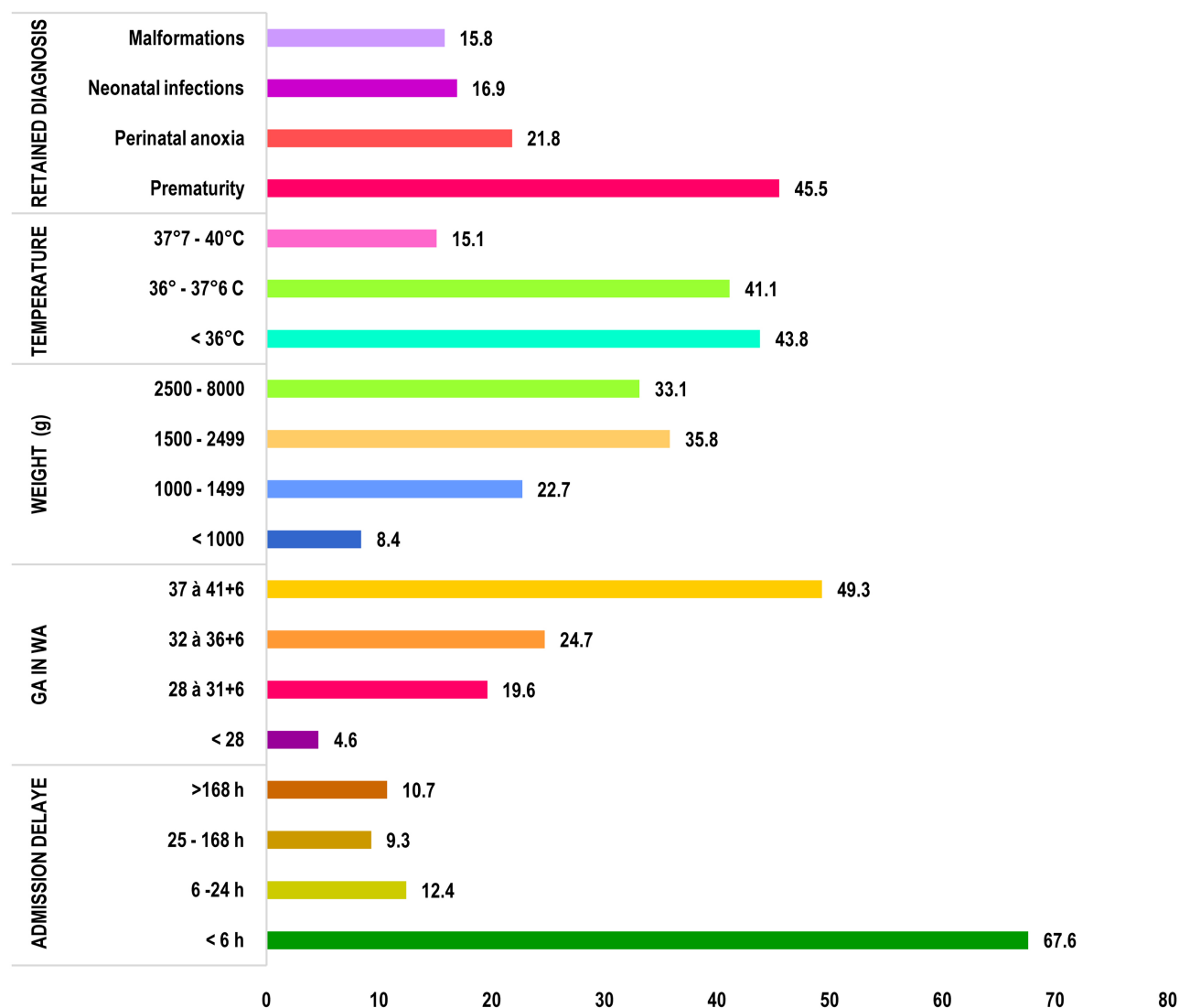
Figure 2. Distribution of functions in patients admission delay, gestational age (GA) of birth weight, the temperature and retained diagnosis.

we observed that the more the newborn was born prematurely the more the risk of death increased, so it was 18.5 times for children under 28th WA (ORa = 18.5; CI = 1.9 - 180; p = 0.012) versus 2.3 times between 28 and 31 WA + 6 (OR = 2.3; CI = 1.4 - 3.8; p = 0.001) compared to this born at term. The same observation for the weight less than 1000 g had 6.6 times risk of death (ORa = 6.6; CI = 1.4 - 29.7; p = 0.015) against 2.2 times between 1000 g and 1499 g (OR = 2.2; CI = 1.3 - 3.7; p = 0.003) relative to normal weight. Compared with normothermia, the risk was 1.9 times for hypothermia (OR = 1.96; CI = 1.3 - 2.9; p = 0.002) than for fever (ORa = 1.9; CI = 1 - 3.5; p = 0.042). Other factors did not influence mortality in our study. For the health structure of origin, we found that there was no statistically significant difference between the base structures (CHC), the reference health centers (RHC), tertiary structures (Hospitals) compared to private structures because the transfer conditions are practically identical. And there

was no statistically significant difference between transport by ambulance and other means used (Table 1).

4. Discussion

4.1. Characteristics of the Country's Reference System, Transfer Conditions, Patient Clinics

In developed countries, there are two types of transfer. Transfer *in utero* to a maternity unit with a neonatal intensive care unit gives better results (mortality, morbidity and long-term sequelae) than a postnatal transfer, especially in a premature newborn [15]. While for the full-term or near-term newborn, postnatal transfer is not always avoidable in cases of unforeseeable per- or postnatal pathology [3] [16]. Our neonatology service at Gabriel Toure University Hospital is the national reference in neonatal care, in recent years we have seen an increase in the number of referrals from 71% to 84% (2007 and 2008-2012) then

Table 1. Distribution according to prognostic factors.

Factors	% among deceased	% among living	Univariate analysis			Logistic regression		
			OR	IC$_{OR}$	p	ORa	ICa$_{OR}$	p
GA in WA								
37 − 41 + 6	32.9	67.1						
<28	96.6	3.4	57.2	7.6 - 428	<0.001	18.5	1.9 - 180	0.012
28 − 31 + 6	53.4	46.6	2.3	1.4 - 3.8	0.001	1.4	0.5 - 3.7	0.495
32 − 36 + 6	29.7	70.3	0.8	0.5 - 1.4	0.561	0.7	0.3 - 1.3	0.253
Admission weight (g)								
2500 - 8000	28.8	71.2						
<1000	89.5	10.5	20.9	7 - 62.6	<0.001	6.6	1.4 - 30	0.015
1000 - 1499	47	53	2.2	1.3 - 3.7	0.003	1.9	0.7 - 4.9	0.179
1500 - 2499	34.8	65.2	1.3	0.8 - 2.1	0.264	1.5	0.9 - 2.8	0.132
Intake temperature								
36˚ - 37.6˚	30.8	69.2						
<36˚	46.7	53.3	1.96	1.3 - 2.9	0.002	1.2	0.7 - 2	0.382
37.7˚ - 40˚	47	53	1.99	1.1 - 3.5	0.017	1.9	1 - 3.5	0.042
Place of birth								
Private structures	44.6	55.4						
Hospitals	30	70	0.9	0.4 - 1.9	0.817	0.8	0.5 - 3	0.543
RHC of Bamako	40.2	59.8	0.5	0.2 - 1.2	0.488	1.3	0.5 - 3	0.543
CHC of Bamako	38.7	61.3	0.7	0.4 - 1.3	0.350	0.8	0.3 - 2.3	0.788
Kati health centers	33.3	66.7	0.7	0.3 - 1.7	0.461	0.8	0.3 - 2.5	0.811
Other Structures-Mali	46.8	53.2	0.6	0.3 - 1.3	0.174	1.5	0.6 - 4.1	0.356
Means of transport								
Ambulance	38.3	61.7						
Other means	44.9	55.1	1.3	0.9 - 1.9	0.194	1.7	0.6 - 4.1	0.126

since 2016 until nowadays we see a reversal of the trend with a gradual decrease in references from around 58% to 53% (2018) with the increase in reference in born [10] [11] [17]. In our study, we found a frequency of 54.3% of hospitalizations. This decrease could be explained by the creation of a pediatric unit with the presence of at least two pediatricians in the reference health centers (RHC) of Bamako and the effective presence of the pediatric activity in maternity at the maternity at the Gabriel Toure University Hospital. The same mode of admission to intensive care and neonatal resuscitation services on all continents and especially in Africa as the neonatal referral represents the main mode of admission [9] [18] [19]. In the organization of the health pyramid of Mali is: at the base the first levels of contact of the population with health structures are: the community health center (CHC) and private structures (practices/clinics). The first referral level is the referral health center (RHC). The second referral level is made up of regional hospitals. The third referral level is made up of national hospitals and certain specialized establishments [7] [8]. In relation to the organization and operation of the system; the circuit of the referred patient is organized so that when called by the peripheral structures (CHC and private structures), the ambulance makes the trip to pick up the patient who will be admitted to the RHC. After examination and evaluation of the clinical picture, a diagnosis is made and treatment decided according to the capacities of the RHC. Cases require higher technical table that the level of RHC are evacuated for continuity of care at a university hospital. Thus we found that 19.3% of references were made directly to the base of the pyramid the Community Health Centers (CHC) and private structures in the neonatal service of the Gabriel Toure University Hospital and 6.7% (30/450) came from one of the tertiary structures (hospitals). Depending on the level of the system, each health facility should be capable of providing all the packets of minimum activities (PMA) [7] [8]. While the reality is different in our health centers, usually the building is not in the standards, lack of equipment, insufficient staff or otherwise lacks competence to practice birth, emergency neonatal care and continuity of care [20]. We found perinatal anoxia (15.3%) as a second reference reason, which shows the benefit of strengthening the skills of staff in neonatal emergency care. This is because childbirth care will have to be reoriented so that the interests of the newborn are duly taken into account [20]. It must start at the first level of the health system, to act on this important factor of neonatal survival which is the place of birth of the newborn [21]. In fact, the transfer of the newborn is indicated if its condition requires care, surveillance or investigations that cannot be carried out in their birth center [3] [6]. The transfer means is chosen according to the severity of the pathology motivating the transfer. The medical ambulance if the newborn is unstable or presents a severe pathology in this context a certain condition must be met (chain of heat, chain of oxygen, chain of sugar, chain of asepsis and chain of information). The non-medical ambulance with a trained nurse and suitable equipment is indicated for the transport of a newborn with mild pathology (no

mechanical ventilation or non-invasive ventilation in progress) [3] [6] [16] [22]. In our country, the newborn was taken into account in the referral/evacuation system only in 2002. In 2007, only 17.4% of referrals received in the service were made by ambulance [9]. In our series, 71.3% of references were made by the ambulance and 26.2% by taxi. And the observation of the high number of transport by taxi made by our peripheral structures, explains the non-respect of the health pyramid by the fact that the ambulance is at the level of the RHC. This increase in the number of ambulance transfers is beneficial but the important thing remains the conditions thereof: the presence on board of a health worker most often not trained in neonatal emergency care and the absence of 'no chains in the ambulances (chains of hot, sugar, oxygen, asepsis and information) [9]. His has been demonstrated in our study that the conveyance was not a determining factor in our context because there was no statistically significant difference between the different means of transport used. Thus, to reduce the morbidity and mortality related to transportation, we must improve the conditions of this [21]. It is therefore urgent in Mali to put in place a means of transport adapted to the condition of the newborn and that our ambulances must be equipped. Neonatal mortality is a heavy burden in developing countries, where newborns continue to die from mostly preventable causes. Reducing neonatal morbidity and mortality requires improving the referral system for newborns in our environment. The four main reasons references found in our study are prematurity (40.2%), anoxia, or perinatal asphyxia (15.3%), malformations (15.3%) and neonatal infections (9.1%) represent most of the causes of neonatal deaths found in the world [18] [19] [23] [24] [25].

4.2. Prognosis of Neonatal References

On the prognostic level, we found a mortality of 40.2%. This high mortality is found in all sub-Saharan countries [26]. Factors contributing to high mortality of neonatal references observed in our study were preterm, low weight, hypothermia and fever. We found a greater danger of death in newborns who were born more prematurely and or with a very low birth weight. The same observation was found in African studies [26]. The high risk of mortality in this population could be explained by their physical and physiological immaturity [27] [28] [29] [30].

Indeed, the poor transport conditions are very harmful to newborns, and the absence of a normthermal environment, ventilation source or a suitable sugar intake can cause irreversible damage in these infants fragile (premature and/or sick) [26] [27] [28] [29] [30]. In our study, we found that any changes in temperature (hypothermia or hyperthermia) would lead to a significant increase in the risk of death. Hypothermia is a real morbidity factor linked to transport found by Rao SK *et al.* 2015, Deepak R *et al.* 2014 and Mathur NB *et al.* 2007 [29] [30] [31]. There is an urgent need to set up a neonatal referral system that meets all the conditions for secure transfer (the means of transport including all the

chains, the appropriate equipment and the competent staff). Without respecting these measures, even in ultra-equipped intensive care units, the survival rate will decrease considerably [3] [15] [16] [21] [30].

5. Limits and Difficulties of the Study

5.1. Methodological Approach

We carried out a cross-sectional study. This type of study makes it possible to take stock of a given question in a given setting, during a given period, taking into account the realities in the field (the hospital). We used data from a survey we carried out in the neonatal ward. The data for this survey were collected retrospectively from a standardized survey form from the medical file and department records.

5.2. Difficulties Encountered

During our study, we were faced with problems of completeness some medical records of newborns in the first munites of life such as the Apgar score. Despite these limitations we were able to carry out our work.

6. Conclusion

The neonatal referral constitutes the major part of our hospitalizations, *i.e.* 54.3% of hospitalizations with still high mortality (40.2%). The top five reasons for neonatal reference were respectively prematurity, perinatal asphyxia, malformations, respiratory distress and neonatal infections. Thus, reducing this burden requires improving the practice of emergency neonatal care in our health facilities. The establishment of a neonatal reference system meets all the conditions of transfer (the means of transport including all the chains, the appropriate equipment and the competent staff) and is adapted to the clinical condition of the newborn.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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